Amendments to the Specification:

Please replace the title of the invention with the following amended title:

~~ENHANCEMENT OF OLIGODENDROCYTE DIFFERENTIATION~~METHOD OF GENERATING OLIGODENDROCYTES FROM NEUROSPHERE CELLS

Please replace the paragraph beginning on page 2, line 15, with the following amended paragraph:

Another approach uses differentiation agents such as retinoic acid to induce neural and glial lineages in EB cultures (Bain et al. 1995; Fraichard et al. 1995). As in newborn brain derived cultures, neural precursors can be further enriched by selecting non-adherent cells growing as floating spheres in defined medium, and expanding them as neurospheres and oligodendrocyte-enriched oligospheres that differentiate after EGF, FGF removal (Zhang et al. 1998; Liu et al. 2000). Human ES cell lines derived EBs also form neural tube like rosettes expandable as floating neurospheres that can be transplanted in vivo or plated on polycationic substrates to differentiate into neurons, astrocytes and oligodendrocytes, the latter developing particularly after treatment with PDGF-AA and T3 (Reubinoff et al. 2001; Zhang et al. 2001). Although cytokines such as ~~LIF~~ leukemia inhibitory

factor (LIF) are known to maintain ES cells in an undifferentiated, multipotent state, it was recently found that LIF allows sparse murine ES cell cultures to develop into neurospheres (Tropepe et al. 2001).

Please replace the paragraph beginning on page 3, line 8, with the following amended paragraph:

CNTF belongs to the interleukin-6 (IL-6) family of cytokines that signal via gp130 either as a heterodimeric receptor with LIF-R (for CNTF, LIF, ~~OSM~~ and oncostatin-M (OSM)) or as a homodimer (for ~~IL-6~~interleukin-6 (IL-6), ~~IL-11~~interleukin-11 (IL-11)) (Taga et al. 1997) for review). There is growing evidence on the importance of gp130 signaling for myelinating cells. In mice, postnatal gene deletion has indicated that gp130 is required to maintain Schwann cell function and myelination in peripheral nerves, in addition to its role in astrocytosis (Betz et al. 1998; Nakashima et al. 1999). With the help of a potent gp130 activating ligand, the IL6R/IL6 chimera in which IL-6 is fused to the extracellular portion of the IL-6 receptor (Chebath et al. 1997), we have previously observed induction of myelin gene expression in embryonic Schwann cells (Haggiag et al. 1999; Haggiag et al. 2001) and activation of myelin gene promoters (Slutsky et al. 2003). Activation of a transgenic MBP gene promoter in mice

brain cultures was observed in response to CNTF (Stankoff et al. 2002) and in similar cortical cultures from newborn rat IL6R/IL6 chimera was more effective than CNTF to increase the development of highly arborized GalC+ oligodendrocytes (Valerio et al. 2002).

Please replace the paragraph beginning on page 11, line 2, with the following amended paragraph:

The present invention embraces the use one or more ~~gp 130~~ gp130 activator, in the manufacture of a medicament for inducing generation of oligodendrocytes from ES, EB and/or NS cells. The ~~gp 130~~ gp130 activator may be added ex-vivo to cultures of ES, EB and/or NS cells, which are thereafter transplanted to a patient. Alternatively the gp130 activator could be injected to a patient before together or after injecting the cells in order to stimulate the in vivo differentiation of ES, EB and/or NS transplants. A preferred in vivo gp130 activator is IL-6 and more preferably IL6R/IL6 chimera. IL6R/IL6 chimera may also be applied for stimulating the generation of oligodendrocytes early progenitors from ES, EB and/or NS cells. Additional gp130 ~~asctivators~~ activators according to the invention are selected from LIF, CNTF, CT-1, OSM, IL-6 and IL-11.

Please replace the paragraph beginning on page 12, line 6, with the following amended paragraph:

The cells according to the present invention comprise cells derived from ~~anyone~~ any one of the above five steps.

Please replace the paragraph beginning on page 17, line 24, with the following amended paragraph:

Without limitation, examples of stringent conditions include washing conditions ~~12°° 20°C~~12-20°C below the calculated Tm of the hybrid under study in, e.g., 2 x SSC and 0.5% SDS for 5 minutes, 2 x SSC and 0.1% SDS for 15 minutes; 0.1 x SSC and 0.5% SDS at 37°C for 30-60 minutes and then, a 0.1 x SSC and 0.5% SDS at 68°C for 30-60 minutes. Those of ordinary skill in this art understand that stringency conditions also depend on the length of the DNA sequences, oligonucleotide probes (such as 10-40 bases) or mixed oligonucleotide probes. If mixed probes are used, it is preferable to use tetramethyl ammonium chloride (TMAC) instead of SSC. See Ausubel, supra.

Please replace the paragraph beginning on page 39, line 28, with the following amended paragraph:

Live cells were stained for O1. After blocking with 5% FCS, anti-O1 mouse IgM Mc antibodies (McAB 344, Chemicon;

1:75) and Fluorescein-conjugated goat anti-mouse IgM (Chemicon; 1:50) were used for 1h at ~~37oC~~37°C in humidified atmosphere, followed by fixation with 5% acetic acid in methanol. In all cases, the nuclear fluorescent dye DAPI (Sigma; 0.05 µg/ml) was added last. Coverslips were mounted in Mowiol (Calbiochem, LaJolla, CA), viewed in an Olympus IX-70 FLA microscope with a DVC-1310C digital camera (DVC, Austin, TX) and images processed by Photoshop. Double stained preparations are shown as overlayed images. A manual count program in the AlphaEase software (Alpha Innotech, San Leandro, CA) was used to measure sizes and enumerate NG2, O4 and GFAP stained cells, as well as total cell nuclei visualized by DAPI.